# HHS STTR RFA-ES-15-005

NOTE: The Solicitations and topics listed on this site are copies from the various SBIR agency solicitations and are not necessarily the latest and most up-to-date. For this reason, you should use the agency link listed below which will take you directly to the appropriate agency server where you can read the official version of this solicitation and download the appropriate forms and rules.

The official link for this solicitation is: http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-15-005.html

Agency:
Department of Health and Human Services

Release Date:
November 24, 2014
Branch:
n/a

Open Date:
November 24, 2014
Program / Phase / Year:
STTR / Phase I / 2015

Application Due Date:
February 13, 2015

Solicitation:
RFA-ES-15-005

Close Date:
February 13, 2015
Topic Number:
RFA-ES-15-005

Description:

Several U.S. government sponsored programs, including the U.S. Tox21 program (http://ntp.niehs.nih.gov/go/tox21) and the U.S. EPA's ToxCast program (http://www.epa.gov/ncct/toxcast/), were developed to expand the scope and throughput of screening compounds for toxicity. A primary focus of these programs is on the use of *in vitro* methods and assays using lower organisms to screen thousands of chemicals for toxicity in order to identify mechanisms of compound-induced biological activity, characterize toxicity pathways, facilitate cross-species extrapolation, and provide input to models for low-dose extrapolation. Data generated by these methods will be used to prioritize compounds for more extensive toxicological evaluation and to develop predictive models for biological response in humans. Current approaches are limited in terms of incorporating genetic variability in toxicity testing and in assessing the effects of chemicals in multiple normal tissue and cell types, relying on immortalized cell lines or primary cell lines derived from tissues. Thus, there is a need for novel, medium- to high-throughput assays (at least a 96-well format) to evaluate the effects of chemical compounds on the differentiation of pluripotent or multi-potent stem cells as well as the effects of chemical exposures on differentiated cell types representative of various *in vivo* tissues. Approaches can include the use of human induced pluripotent stem (iPS) cells, approved human embryonic stem (ES) cell lines, or ES or iPS cells derived from genetically characterized mouse strains. Assays should be able to measure the effects of toxicants on the differentiation process and/or on the differentiated cells themselves; cell types of high priority include but are not limited to cardiomyocytes, neural cells, hepatocytes, endothelial cells, lung (airway or alveolar) cells, and hormonally-responsive tissues such as

reproductive tissues or breast epithelial cells.

Approaches can include:

- Assays that evaluate the ability of chemicals to alter the ability of ES/iPS cells to be differentiated into various cell types
- Human iPS or mouse ES/iPS cell line panels to incorporate genetic variation into toxicity screening.
- Engineered stem cell lines to simulate the common genetic variants in human disease that would predispose to increased sensitivity to toxicants (e.g., Parkinson's Disease, autism, breast cancer, or other relevant disease models)
- High-content screening or 'omics-based assays (metabolomics, proteomics, epigenetic marks, or transcriptomics) for toxicant-induced effects using differentiated cell types derived from pluripotent or multi-potent cells.

Assays should be developed using toxicants or reference compounds that are appropriate to the endpoints and purposes of that assay. High priority should be given to including some compounds that are currently in the Tox21 10k library (see http://www.epa.gov/ncct/dsstox/sdf_tox21s.html). The Tox 21 library contains samples from commercial sources and includes industrial chemicals, pesticides, food additives, toxicity reference chemicals, and drug compounds.

Applications may develop assays using mouse embryonic stem cells, adult human stem cells, induced pluripotent stem (iPS) cells, or human embryonic stem cell (hESC) lines that are approved for NIH funding as indicated in the NIH Human Embryonic Stem Cell Registry (http://grants.nih.gov/stem_cells/registry/current.htm). If an hESC application proposes research for which the specified hESC line(s) has not yet been approved, only restricted awards will be issued until the specified hESC line(s) is approved.

For this FOA, assays should be developed using only human ES, iPS or adult stem cells or ES/iPS cells from genetically-characterized mouse strains. Applications proposing assay development using cells derived from rat strains or other animal models are not responsive to this FOA.